the conjugate binds to a chemokine receptor resulting in internalization of the targeted agent in cells bearing the receptor.

39. A method of effecting gene therapy, comprising contacting cells bearing chemokine receptors with the conjugate that comprises a targeted agent and a chemokine receptor targeting agent, or a portion thereof, wherein the conjugate binds to a chemokine receptor resulting in internalization of the targeted agent in cells bearing the receptor [of claim 1], wherein the targeted agent is a nucleic acid.

REMARKS

Any fees that may be due in connection with this paper or with this application during its entire pendency may be charged to Deposit Account No. 08-1641. If a Petition for extension of time is needed, this paper is to be considered such Petition.

Claims 25-40 and 42-64 are presently pending in this application. Claims 1-24 and 41 have been cancelled without prejudice or disclaimer, and a divisional application claiming the non-elected subject matter in this case was filed on December 2, 1999 (attorney docket no. 25020-601C). Claims 29 and 38 are amended and rewritten as independent claims incorporating all limitations of cancelled base claim 1. Claims 42-64 have been added. These claims find basis, for example, in original claims 1-24. Therefore, no new matter has been added.

A substitute Sequence Listing (paper and disk copies), a DECLARATION of Stephanie Seidman regarding the addition of subject matter previously incorporated by reference, and a copy of the Notice to Comply accompany this response.

The specification has been amended to indicate entries that have been added to the Substitute Sequence Listing attached herewith, namely, SEQ ID NOS. 89-93. These sequences are incorporated by reference in the specification as originally filed. SEQ ID NOS. 89-92 are described in Clark-Lewis

et al. (1995) *J Leukoc Biol* 57, 703-11, cited at page 2, line 20 of the specification as originally filed, and SEQ ID NO. 93 is described in Shirozu *et al.*, *Genomics*, *28*: 495-500. 1995, cited at page 6, line 24 of the specification as originally filed. The specification incorporates all cited references in their entirety (see, *e.g.*, page 30, lines 1-8). Hence the added sequences do not constitute new matter. A DECLARATION of Stephanie Seidman attesting to the identify of the sequences provided in the references and included in the SEQ LISTING accompanies this response.

SEQ ID NO. 67 disclosed at page 73, line 4 of the specification was inadvertently described as the sequence of the chemokine MCP-2, instead of the chemokine MCP-3. This has been corrected. The error is evident because SEQ ID NO. 67 disclosed in the Sequence Listing as originally filed, and as filed in the Substitute Sequence Listing attached herewith, encodes amino acids identical to those set forth in Table 3 and SEQ ID NO. 22 that include the amino acid sequence of MCP-3. SEQ ID No. 21 sets forth the amino acid sequence of MCP-2. Comparison of the two reveals that SEQ ID No. 67 encodes MCP-3, not MCP-2. Therefore no new matter has been added.

All other amendments to the specification correct obvious typographical, grammatical, spelling and formatting errors. No new matter has been added.

Attached herewith is a substitute Sequence Listing, disk and paper copies, a Verified Statement that the content of the paper and computer readable copies are the same, and a copy of the Notice to Comply with Requirements for Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures.

The substitute Sequence Listing differs from the Sequence Listing as originally filed in that the Substitute Sequence Listing corrects the errors noted in the Raw Sequence Listing Error Report accompanying the Notice to Comply, as follows:

at page 1, Line 17 of the Raw Sequence Listing, the base count of 43 has been changed to 49, as noted in the Notice to Comply;

at page 1, Line 20 of the Raw Sequence Listing, the base count of 82 has been changed to 88, as noted in the Notice to Comply;

at page 3, Line 97 of the Raw Sequence Listing, the duplicated line has been deleted; and

at page 4, Line 100 of the Raw Sequence Listing, the Artificial Sequence (SEQ ID NO 10) has been described as noted in item 12 on the Error Summary Sheet. SEQ ID NOS. 1-9 have been described in a similar manner.

As noted at the bottom of Page 5 of the Raw Sequence Listing, SEQ ID NO. 68, which has an amino acid Xaa in the sequence, has been explained as to the identity of Xaa, and as to the "repeat" nature of the sequence.

The substitute Sequence Listing also differs from the original in that SEQ ID NOS. 71-93 have been added to it. SEQ ID NOS. 71-88 are the amino acid sequences encoded by the nucleotide sequences corresponding to SEQ ID NOS. 52-67 and 69-70, respectively, which were in the Sequence Listing as originally filed. No new matter has been added. SEQ ID NOS. 89-93 are incorporated by reference in the specification as originally filed. Specifically, SEQ ID NOS. 89-92 are described in Clark-Lewis *et al.* (1995) *J Leukoc Biol* 57, 703-11, cited at page 2, line 20 of the specification as originally filed, and SEQ ID NO. 93 is described in Shirozu *et al.*, *Genomics*, *28*: 495-500. 1995, cited at page 6, line 24 of the specification as originally filed. Therefore, the addition of SEQ ID NOS. 89-93 to the substitute Sequence Listing does not constitute matter which goes beyond the disclosure in the application as originally filed.

The description of SEQ ID NO. 67 has been amended to read as "MCP-3" instead of "MCP-2", which was the description in the Sequence Listing as originally filed. This error is of an inadvertent and obvious nature because SEQ ID NO. 67 disclosed in the Sequence Listing as originally filed, and as filed in the substitute Sequence Listing attached herewith, is identical to amino acids set

forth in SEQ ID No. 22 and in TABLE 3 as the sequence of MCP-3, not MCP-2, which is set forth in SEQ ID No. 21. Simple comparison of the amino acid sequences reveals that SEQ ID No. 67 encodes MCP-3, not MCP-2. Therefore, no new matter has been added.

The substitute Sequence Listing contains no new matter, or matter which goes beyond the disclosure in the application as originally filed. Accordingly, entry of the Substitute Sequence Listing into the file history of the above-captioned application is respectfully requested.

Therefore, no new matter has been added.

TRAVERSE OF THE REQUIREMENT FOR RESTRICTION

The requirement for Restriction as between groups II and III is respectfully traversed as follows.

Groups II and III

Group II is directed to methods of treatment and includes claims, such as claim 30, which, with the lanuage of the base claim included reads as follows:

30. [The method of claim 29] A method for treating inflammatory responses associated with activation, proliferation and migration of immune effector cells, comprising administering a conjugate of claim 1 to an animal mammal, whereby an inflammatory response associated with activation, proliferation migration or the immune effector cells is inhibited, **wherein the disorder or disease state comprises secondary tissue damage**.

Group III is claim 40, which reads as follows:

40. A method for treating secondary tissue damage and associated disease states, comprising administering to a subject in need thereof an effective amount of a therapeutic agent that inhibits the proliferation, migration or physiological activity of secondary tissue damage-promoting cells.

Comparison of these claims reveals that claim 30 is within the scope of claim 40. If the claims are restricted into these two groups, applicant ultimately could be granted two patents. If a patent with claim 30 issues before

a patent, it could not be held to constitue obviousness-type double patenting cannot over an application with claim 40 in it.

See MPEP 806, paragraph 3, which states:

> [w]here inventions are related as disclosed but are not distinct as claimed, restriction is never proper. Since, if restriction is required by the Office double patenting cannot be held, it is imperative the requirement should never be made where related inventions as claimed are not distinct.

See, also MPEP 804.01, which states:

> 35 U.S.C.121, third sentence, provides that wherein the Office requires restriction, the patent of either the parent or any divisional application thereof conforming to the requirement cannot be used as a reference against the other. This apparent nullification of double patenting as ground of rejection or invalidity in such cases imposes a heavy burden on the Office to guard against erroneous requirements for restriction where the claims define essentially the same inventions in different language and which, if acquiesced in, might result in the issuance of several patents for the same invention.

Therefore reconsideration of the requirement for restriction as between groups II and III is respectfully requested.

* * *

In view of the above amendments and remarks, examination of the application on the merits is respectfully requested.

Respectfully submitted,
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